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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/576,901	04/20/2006	Michael Joseph Coghlan	X-16398	5935

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EXAMINER	
SOLOLA, TAOFIQ A	
ART UNIT	**PAPER NUMBER**
1625	

NOTIFICATION DATE	DELIVERY MODE
10/12/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patents@lilly.com

Office Action Summary	Application No.	Applicant(s)	
	10/576,901	COGHLAN ET AL.	
	Examiner	Art Unit	
	Taofiq A. Solola	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) 1-19 and 21 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) 1-9,14-19 and 21 is/are rejected.

7)☐ Claim(s) 10-13 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 1.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Claims 1-19, 21 are pending in this application.

Claims 20, 22-23 are cancelled.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 19, 21 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

"'In the context of determining whether sufficient "utility as a drug, medicant, and the like in human therapy" has been alleged, it is proper for the examiner to ask for substantiating evidence unless one with ordinary skill in the art would accept the [compounds and the utilities] as obviously correct." *In re Jolles*, 628 F.2d 1327, 1332 (Fed. Cir. 1980), citing *In re Novak*, 306 F.2d 924 (CCPA 1962); see 340 F.2d 974, 977-78 (CCPA 1965). "A specification disclosure which contains a teaching of the manner and process of making and using the invention . . . must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support." *In re Brana*, 51 F.3d 1560 (Fed. Cir. 1995), Id. at 1566, quoting *Marzocchi*, 439 F.2d 220, 223 (CCPA 1971); *Fiers v. Revel,* 984 F.2d 1164, 1171-72 (Fed. Cir. 1993), quoting *Marzocchi*, 439 F.2d at 223; see also *Armbruster*, 512 F.2d 676, 677 (CCPA 1975); *Knowlton*, 500 F.2d 566, 571 (CCPA 1974); *Bowen*, 492 F.2d 859 (CCPA 1974); *Hawkins*, 486 F.2d 569, 576 (CCPA 1973). Where there is "no indication that one skilled in the art would accept without question [the instant compounds and method of use] and no evidence

has been presented to demonstrate that the claimed products do have those effects *Novak*, 306 F.2d at 928, an applicant has failed to sufficiently demonstrate sufficient utility and therefore cannot establish enablement."' *In re Rasmusson,* 75 USPQ2d 1297 (CAFC 2005). The claimed utilities are not enabled for the following reasons:

For rejection under 35 U.S.C. 112, first paragraph, the following factors must be considered. *In re Wands*, 8 USPQ2d 1400, 1404 (CAFC, 1988):

"The factors to be considered [in making an enablement rejection] have been summarized as a) the breadth of the claims, b) the nature of the invention, c) the state of the prior art, d) the relative skill of those in that art, e) the predictability or unpredictability of the art, f) the amount of direction or guidance presented, g) the presence or absence of working examples, h) the quantity of experimentation necessary. The breathe of the claims encompass many compounds. The nature of the invention is using the compounds as pharmaceuticals. Applicant claims using the compounds for treating all the various diseases listed in the claims. However, the specification fails to disclose conclusive evidence linking the diseases with the compounds.

There is no prior art claiming compounds useful for treating all the listed diseases (one-size-fits-all). Even then, such would be contrary to established scientific principles because the listed diseases arise from various mechanisms. The specification on pages 47-48 disclosed table of results from mineralocorticoid (MR) and glucocorticoid (GR) receptors binding assays. But, there is no discussion, explanation and establishment of nexus between the results and each of the diseases in claims 19 and 21. Hence, there is no absolute predictability or established correlation between the diseases and inhibitions of MR and GR. The uncertainty presents one of ordinary skill in the art with obstacles and prevents her from accepting the claims on their face. The level of ordinary skill in the art of pharmaceuticals is high. It is well

established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved". See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

The statements on page, line 30 to page 5, line 2, are mere speculations. In support thereof, applicant relies on other publications as well US patent 6,166,013. The patent fails to disclose nexus between GR inhibitors and each disease in claims 19 and 21. The patent discloses very few diseases. The patent and the referenced publications in the instant application are not incorporated by reference in accordance to the MPEP, which states as follows:

A mere reference to another application, publication or patent is not an incorporation of anything therein into the application containing such reference for the purpose of satisfying the requirement of 35 USC 112, first paragraph. *In re de Seversky,* 474 F.2d 671, 177 USPQ 144 (CCPA 1973). Particular attention should be directed to the subject matter and the specific portions of the referenced document where the subject matter being incorporated may be found. MPEP 608.01(p).

If the document is a pending US application: prior to allowance of an application that incorporates essential material by reference to a pending US application, if the referenced application has not been published or issued as a patent, applicant is required to amend the disclosure of the referencing application to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating the amendment consists of the same material incorporated by reference in the referencing application. MPEP 608.01(p).

The requirement of 35 USC 112, is not what is known or obvious to one of ordinary skill in the art but a "full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same",

Lookwood v. American Airlines Inc. 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed Cir. 1997). Given the limited guidance in the specification one of ordinary skill in the art would have to perform significant amount of experiments to make and use the invention as claimed.

MPEP 2164.01(a) states, "[a] conclusion of lack of enablement means that, based on the evidence regarding any of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 6-8, 15-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Tewari et al., *Studies on Betaine Decomposition of Arsonium Ylides*, Anorg. Chem. Org. Chem., (1980), Vol. 35 (1) pp. 95-98.

Tewari et al., disclose compounds 11a and 13a and their compositions. See page 96 and table 1, page 97.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to

a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-9, 14-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tewari et al., *Studies on Betaine Decomposition of Arsonium Ylides*, Anorg. Chem. Org. Chem., (1980), Vol. 35 (1) pp. 95-98, and Tagaki et al., J. Am. Chem. Soc. (1983), Vol. 105(14), pp. 4676-4684, individually in view of King, Med. Chem.: Principle and Practice (1994), p. 206-208.

Applicant claims compounds of formula I and their compositions, wherein Z is S, O, or CH_2 and R3 is alkoxy.

Determination of the scope and content of the prior art (MPEP 2141.01)

Tewari et al., teach similar compounds and composition thereof wherein Z is CH_2 or O. See compounds 11a and 13a. (Claims 1-5, 6-8, 15-18).

Tagaki et al., teach similar compounds and composition thereof wherein Z is CH_2 and R3 is alkoxy. See compounds 3 and 6. (Claims 1-9, 14-18).

Ascertainment of the difference between the prior art and the claims (MPEP 2141.02)

The difference between the instant invention and that of Tewari et al., is that applicant claims Z is S, O, or CH_2 instead of Z is CH_2 or O by Tagaki et al..

The difference between the instant invention and that of Tagaki et al., is that at position R3 applicant's compound is a position isomer of Tagaki et al.'s compounds. Also, compound 6 of Tagaki et al has alkyl instead of H by applicant when Z is CH_2.

Finding of prima facie obviousness---rational and motivation (MPEP 2142.2413)

However, King teaches that replacement of CH_2 or O with S is expected to produce compounds having similar biological activity (bioisosterism). See page 208, ring equivalents. See also, *Ex parte Engelhardt,* 208 USPQ 343 (Bd. Pat. App. & Int., 1980); *In re Merck,* 231 USPQ 375 (Fed. Cir., 1986).

Also, H and alkyl are art recognized equivalents. *In re Lincoln*, 126 USPQ 477, 53 USPQ 40 (CCPA, 1942); *In re Druey*, 319 F.2d 237, 138 USPQ 39 (CCPA, 1963); *In re Lohr*, 317 F.2d 388, 137 USPQ 548 (CCPA, 1963); *In re Hoehsema*, 399 F.2d 269, 158 USPQ 598 (CCPA, 1968); *In re Wood*, 582 F.2d 638, 199 USPQ 137 (CCPA, 1978); *In re Hoke*, 560 F.2d 436, 195 USPQ 148 (CCPA, 1977); *Ex parte Fauque*, 121 USPQ 425 (POBA, 1954); *Ex parte Henkel*, 130 USPQ 474, (POBA, 1960).

A novel and useful compound, which is an isomer of a compound of prior art, is prima facie obvious. *In re Norris,* 84 USPQ 458 (1950).

Therefore, the instant invention is prima facie obvious from the teachings of the prior arts. One of ordinary skill in the art would have known to make all the changes to the compounds of the prior arts at the time the invention was made. The motivation is from knowing that H and alkyl are equivalents, replacing CH_2 or O with S would produce compounds having similar biological properties, and from the expectation that position isomers would have similar biological and/or chemical properties.

Objection

Claims 10-13 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taofiq A. Solola, PhD. JD., whose telephone number is (571) 272-0709.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, can be reached on (571) 272-0867. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

TAOFIQ SOLOLA
PRIMARY EXAMINER
Group 1625

September 26, 2007

The claims